

national introduction of olestra-containing foods. The petitioner found that while the absolute number of reports increased when olestra-containing foods were first introduced into test markets, the reporting rate (reports per amount of product sold) declined over time. The petitioner also found that over time the absolute number of reports declined and eventually reached a plateau. The greatest number of reports the petitioner received over a four month period was 4,951 in 1998 at the national introduction of olestra-containing snacks. The petitioner stated in its initial reports on passive surveillance that it is common to receive calls and complaints for products. At the start of national marketing the reporting rate was one report for approximately 100,000 servings sold, and 2 years later the reporting rate was one report for approximately 1 million servings sold.

The petitioner analyzed the data from its passive surveillance efforts and found no trend toward increased symptoms with increased consumption; no trend towards increased severity with increased consumption; and no difference in severity by age group or gender. The petitioner's Olestra Postmarketing Surveillance Committee reviewed reports using an algorithm developed to assess the likelihood that an effect was caused by olestra. Using this algorithm, P&G's committee concluded that many reports were not likely to be related to olestra and no serious reports could be attributed to olestra (Docket No. 00F-0792, submission dated March 3, 2000). Based on the nature of the complaints received, the petitioner designed subsequent studies to address, in part, issues arising from consumers' anecdotal reports after eating olestra-containing foods.

In the 1996 final rule, FDA determined that the use of olestra was safe based on results from the preapproval safety studies. FDA stated in the 1996 final rule (61 FR 3118 at 3168) that P&G's plans to continue to study the consumption and effects of olestra were both prudent and responsible. FDA expected, based on results of the preapproval studies, that some reports concerning GI upset, such as loose stools and abdominal cramping, would be collected through a system of passive surveillance. FDA also considered that postmarket passive surveillance had the potential to detect low frequency and unexpected events because postmarket passive surveillance involves the entire population that consumes a product.

FDA reviewed the reports of effects attributed to olestra and found that the majority of reports received concern GI effects such as loose stools and abdominal cramping. Other symptoms were reported at lower frequencies.

FDA recognizes that passive surveillance data such as those collected by P&G have utility but are limited in that they do not allow for the determination of a causal association between the product consumed (*i.e.*, olestra-containing foods) and effects reported. Such reports can, however, lead to hypothesis generation about why specific effects are occurring. This may then result in the development of studies used to test these hypotheses (Ref. 4).

FDA reviewed reports of effects associated with ingestion of olestra that led consumers to seek medical attention. Where possible, the agency reviewed medical records that were obtained directly from individuals who reported the effect or that were obtained through P&G and CSPI (Refs. 5 and 6). At the 1998 FAC meeting, FDA presented its analysis of the medical reports received up to that time. Among the reports discussed was a case where a consumer had undergone an appendectomy and associated this with consuming an olestra-containing food. The pathology diagnosis at the hospital noted that there were minimal inflammatory changes. FDA obtained a medical release from the patient in order to examine the pathology slides from the appendectomy, which were read independently by four FDA pathologists, all of whom confirmed the presence of inflammatory cells throughout the wall of the appendix meriting a diagnosis of acute appendicitis.<sup>14</sup> In many other of the medical records reviewed, physicians attributed patient symptoms to an etiology other than olestra, or did not provide an etiology. There were cases where physicians did attribute symptoms to olestra, but the limitations of passive surveillance make it difficult, if not impossible, to draw definitive conclusions about causality based on the review of individual medical records.

#### 3. Postmarket Surveillance Reports From CSPI

CSPI has periodically submitted to FDA reports of effects allegedly associated with the consumption of olestra (Docket No. 87F-0179). The complaints were gathered initially in test markets by calls to an advertised toll-free telephone line, and gathered

subsequently through CSPI's Internet site.

FDA analyzed the reports from CSPI and compared the information and analysis to the information and analysis of the reports submitted to FDA by P&G. FDA noted that the reports received by CSPI were very similar in nature, type of complaint, and amount consumed as the reports by P&G.<sup>15</sup> As discussed previously, passive surveillance has limited utility in determining causality.

#### 4. Comments Regarding Consumer Reports

FDA received comments about reports of effects that consumers attributed to olestra. FDA considered these comments and responds in the following section of this document.

(Comment 1) One comment from an individual consumer to the current petition reported that a family member who had Addison's disease suffered gastric cramps and diarrhea, laid down, went into an Addisonian crisis, and died after consuming olestra-containing potato chips. The comment did not provide any further information regarding the death mentioned. CSPI forwarded to the agency the medical record of an Addison's disease patient who had reportedly consumed olestra-containing potato chips prior to death. The patient who died was diagnosed as having Addison's disease (adrenocortical insufficiency) and hypothyroidism in 1989. FDA believes, based on several factors, that the comment and medical record provided by CSPI refer to the same person.

FDA reviewed the medical record forwarded by CSPI. This patient collapsed suddenly after experiencing a bout of gastroenteritis, and reportedly consumed olestra-containing chips prior to the bout of gastroenteritis. An autopsy showed that the adrenal glands could not be identified and noted a finding of Hashimoto's thyroiditis. The medical record did not provide any information regarding the gastroenteritis experienced prior to death.<sup>16</sup> Due to the lack of information contained in the medical record, the agency was unable to determine whether the ingestion of olestra had any role in this patient's illness or death (Ref. 5).<sup>17</sup>

<sup>15</sup> Transcript, vol. 1, pp. 258-270.

<sup>16</sup> The Certificate of Death lists acute cardiorespiratory arrest as the immediate cause of death with autoimmune adrenocortical deficiency syndrome as the underlying cause leading to the immediate cause of death. Other significant conditions contributing to death but not resulting in the underlying cause include mitral valve prolapse and Hashimoto's thyroiditis.

<sup>17</sup> FDA investigated the death mentioned in the comment. As part of the investigation, FDA spoke with the patient's spouse and the patient's co-

<sup>14</sup> Transcript, vol. 1, pp. 271-276.